REMARKS

Reconsideration and continuing examination of the above-identified application is respectfully requested in view of the amendments above and the discussion that follows.

Claims 1-20, 22-26 and 28-44 are withdrawn due to their being directed to non-elected subject matter. Claims 21 and 27 have been amended pursuant to the Examiner's helpful suggestion. Claims 21 and 27 are in the case and are before the Examiner.

I. The Amendments

The specification has been amended pursuant to the Examiner's helpful suggestion for use of the headings. The text under the heading CROSS-REFERENCE TO RELATED APPLICATIONS provided citations to two German and a PCT filing noted in the Application Data Sheet provided when the application was filed. An amended, shortened ABSTRACT is provided in an attached page at the end of this paper.

Claims 21 and 27 have been amended pursuant to the Examiner's helpful suggestion. No new matter has been added.

II. The Action

A. Drawings

The Action noted that separate drawings were required. A further set of drawings is being filed separately along with this paper.

B. Rejection Under 35 USC §101

Claims 21 and 27 were rejected as allegedly not showing the "hand of man". The Action suggested corrective language and although it cannot be agreed that the hand of man was not shown, the claims have been appropriately amended to speed prosecution.

C. Rejection Under 35 USC §112, First Paragraph

Claims 21 and 27 were rejected under the first paragraph of Section 112 as allegedly not complying with the written description requirement aspect of that paragraph. The Action asserts that the claimed fragments must possess the same immunological activity as the full length polypeptide, but there is no recitation as to what part of the full length polypeptide is essential to that activity and is therefore conserved. This basis for rejection cannot be agreed with and is respectfully traversed.

It is first submitted that there is no mention in the claim of the immunological properties of a full length polypeptide; i.e., a full length or a full length KLH1. There is, however, a detailed explanation that the immunological properties of a haemocyanin domain (here domain h of KLH1) can be determined using standard methods, e.g. crossed immunoelectrophoresis. Such immunoelectrophoresis is disclosed throughout the present examples ("crossed IE") and is even well known in the prior art (see Söhngen et al as cited by the Examiner and as also cited in the present specification at page 27, first paragraph). The crossed IE method uses well known antibodies (see e.g., page 23, last paragraph). As a consequence of those disclosures, the situation here is

different from that in *Fiers v. Ravel* 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) or Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016 (Fed. Circ. 1991) how to make where hopped for inventions were discussed.

Claims 21 and 27 encompass only those fragments that show the same immunological activities such those of KLH1, domain h (SEQ ID NO:73). This means, the immunological activity of such a fragment (e.g. in a crossed IE method) is the immunological activity of a polypeptide of SEQ ID NO: 73. The skilled person would immediately know from the present specification that the present applicants had not only possession of recombinant polypeptides comprising SEQ ID NO:73 but also of fragments thereof that were obtained by a few amino acid deletions such that the immunological activity of SEQ ID NO:73 is retained (as e.g. determined in a crossed IE by the same antibody response pattern obtained for SEQ ID NO:73 or fragments thereof).

D. Rejection Under 35 USC §102

Claims 21 and 27 were rejected under 35 USC §102 as allegedly anticipated by the teachings of Söhngen et al. (hereinafter Söhngen). It is specifically asserted that Figure 6 at page 606 shows the isolation of the h subunit of KLH1 derived from *M. crenulata*. This basis for rejection cannot be agreed with and is respectfully traversed.

It is first noted that Söhngen does not teach the isolation of purified homogeneous subunits of KLH1, but only an analysis to determine the formerly unknown subunit organization of KLH1. Figure 6 that is on page 607 of Söhngen is an SDS-PAGE analysis of the KLH1 subunits and their fragments obtained after limited proteolysis with a variety of enzymes. Although it is

possible with this analytical method (in combination with HPLC and SDS) to identify the subunits of KLH1, it is not possible to obtain isolated protein as is presently claimed.

The fragments obtained by limited proteolysis always represent a mixture of different sequences. Even after anion exchange HPLC or SDS, there is always a 10% molecular weight tolerance of the obtained "isolated" fragments using the Gebauer technique. The obtained fragments are sufficient to characterize the subunits of KLH1 and the sequencing of about 10 amino acid residues of each domain. However, the examples obtained by that method are not pure enough and not available in an amount sufficient to provide homogeneous, highly pure domains as can be achieved from the claimed subject matter of claims 21 and 27.

Thus, before this invention, one could not previously have been able to provide the isolated polypeptides of the claims. The impossibility of the isolation of a homogeneous polypeptide from a natural source and the complexity of the naturally occurring polypeptide prevents sequencing of KLH1 and each single domain thereof. The naturally occurring KLH1 is a very complex mixture of different oligomeric species comprising didecamers as well as polymeric microtube-like structures. Accordingly, nowhere in nature is a single isolatable protein of these claims. This basis for rejection should therefore be withdrawn.

III. Further Argument

Because of the complex nature of the KLH mixtures that are available in nature, a skilled worker could not simply sequence the native protein -- there was none. In addition, in *M. crenulata,* there is no cDNA detectable that encodes KLH1.

Therefore, as noted at page 3 of the specification, cDNA could not be isolated from this animal. Accordingly, an alternative route was needed to obtain the claimed subject matter.

No primers or probes were known at the time the present invention was made. The alternative route that was successful here was to use probes designed from the closely related species *Haliotis tuberculata* that produces a similar haemocyanin subspecies that is designated Hth herein. It was only after designing cDNA primers and probes from Hth was the provision of cDNAs for KLH possible. This being the case, there was no reasonable expectation of success in making the claimed invention at the time it was made. As such, not only is the present invention not anticipated, it would also not have been obvious to a worker of ordinary skill at the time the invention was made.

IV. Information Disclosure Statement

The Action noted that European Patent Application EP 0 252 829 A1 was not considered because there was no English version or abstract provided. It has now been learned that EP 0 252 829 A1 has matured into US Patent No. 5,021,560. That US Patent is noted on the enclosed Form PTO-1449 and it is understood that being an issued US Patent, a physical copy is not required to be provided.

V. Summary

Claims 1-20, 22-26 and 28-44 are withdrawn due to their being directed to non-elected subject matter. Pending claims 21 and 27 have been amended pursuant to the Examiner's helpful suggestion. Each basis for rejection or objection has been dealt with and overcome or otherwise made moot.

It is believed that this application is in condition for allowance of all of the pending claims. An early notice to that effect is earnestly solicited.

No further fee or petition is believed to be necessary. However, should any further fee be needed, please charge our Deposit Account No. 23-0920, and deem this paper to be the required petition.

The Examiner is requested to phone the undersigned should any questions arise that can be dealt with over the phone to expedite this prosecution.

Respectfully submitted,

By _____
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Enclosure
- Petition and fee
- Form PTO-1449
- Replacement drawings
- Abstract Page

CERTIFICATE OF MAILING

I hereby certify that this Reply and Amendment, Abstract page, Form PTO-1449, and Replacement Drawings, along with a Petition for an Extension of Time and its fee are being deposited with the United States Postal Service with sufficient postage as First Class Mail in an envelope addressed to: MAIL STOP AMENDMENT, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450, on September 19, 2005.

By _____
Edward P. Gamson